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EXAMINER	
LEFFERS JR, GERALD G	

ART UNIT	PAPER NUMBER
1636	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/424,459	PEETZ, WOLFGANG	
	Examiner	Art Unit	
	Gerald G Leffers Jr.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *2,3,6,7,9,10,13,14,16-18 and 20-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,5,8,11,12,15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 March 2000* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The request filed on 4/22/03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/424,458 is acceptable and a CPA has been established. An action on the CPA follows.

Applicants have not filed a response to the action mailed 10/22/02 as Paper No. 16. The action mailed in Paper No. 16 is repeated below. Because a new grounds of rejection is made herein, this action is not final.

Election/Restrictions

Applicant's election with traverse of Group II (claims 1-2, 4-5, 8, 11-12, 15 and 19; claims drawn to SEQ ID NO: 4-5) in Paper No. 14 is acknowledged. The traversal is on the ground(s) that taken as a whole, the claims of the different groups represent a single inventive concept over the prior art warranting examination in a single application. The response indicates that all of the proteins encoded by the four main groups are regulatory proteins and, therefore, they merely represent different aspects of a single invention. This line of reasoning, that the different groups merely represent different aspects of the same invention when each claim is considered as part of the whole, seems perilously close to an admission that each of the inventions represented by the different groups makes obvious the inventions of the other group. However, this line of argument is not found persuasive because the different proteins encoded by the different nucleic acids of the invention have distinct structural/functional properties that confer distinct special technical features to the nucleic acids and proteins of the invention. With

regard to a novel contribution to the art, regulatory proteins of many different types, including those general categories claimed herein have been long known in the art.

Upon further consideration, it appears that claim 2 was inadvertently included in Group II when it should have been grouped with those claims drawn towards zinc finger proteins. The elected invention is directed towards a guanine nucleotide exchange factor, which does not properly belong in Group II. For example, the zinc finger proteins described in the instant specification are not also guanine nucleotide exchange factors. Nor does the prior art appear to describe any zinc finger proteins (i.e. typically DNA-binding transcription regulators) as also being a guanine nucleotide exchange factor (i.e. typically membrane proteins involved in signal transduction pathways). Accordingly, claim 2 has been withdrawn from consideration along with the other zinc finger protein claims.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-24 are pending in this application, with claims 2-3, 6-7, 9-10, 13-14, 16-18 and 20-24 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14. Claims 1, 4-5, 8, 11-12, 15 and 19 are under consideration.

Drawings

Applicants' attention is directed towards the attached photocopy of a PTO Form 948 that comprises objections to the drawings of the instant application made by the Draftsperson.

Appropriate correction is required in the time period specified for response to the instant Office Action (see 37 C.F.R 1.85(a)).

Claim Objections

Claims 1, 4-5, 8, 11-12, 15 and 19 are objected to because of the following informalities: the claims are directed to nonelected embodiments (i.e. to nucleic acid sequences other than the mcg7 gene and protein described by SEQ ID NOS: 4-5). Appropriate correction is required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 5 and 12 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. This grounds of rejection is limited to those embodiments recited in the Markush groups of nucleotide sequences in these claims that are limited to SEQ ID NOS: 4 & 5.

SEQ ID NOS: 4 & 5 appear to be novel in the art and, therefore, do not have a well-established utility.

The rejected claims are directed towards various nucleic acids that are permutations of the nucleic acid sequence set forth in SEQ ID NO: 4 or which encode the polypeptide described by SEQ ID NO: 5. The specification discloses that SEQ ID NO: 4 was obtained from cDNAs and compared to known sequences for homology. The specification identifies the nucleic acids as encoding a protein having guanine nucleotide exchange factor activity based on homology to

other known sequences. However, proteins comprising such a guanine nucleotide exchange domain can have very different functions and the specification does not appear to provide a basis for one of skill in the art to visualize what function the whole protein may have in an actual cell (e.g. what factors does it bind or interact with and what events follow such interaction? Activation of what pathways?).

The prior art does not teach that it is a trivial matter to determine protein structure function relationships based upon homology alone. The relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). The whole reference teaches about the unpredictability in the art concerning protein structure, and failures to make it predictable. Thus, as taught by Berendsen, it is unlikely that one can assign a definite specific function to MCG7 based upon limited homology to proteins known in the art at the time of filing. Any putative, specific function assigned to MCG7 would need experimental confirmation and would therefore not be substantial. Therefore, based upon the unpredictability in the art with regard to predicting protein function/structure relationships, and given the lack of teachings of a specific or substantial utility in the instant specification and prior art, one of skill in the art would reasonably conclude there is not a specific and substantial utility for the claimed nucleic acids.

Claims 5 and 12 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 19 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim is directed to a diagnostic method for detecting a condition caused by or facilitated by an aberration in mcg7, or a propensity to develop the condition. The critical element of the invention is a disease or condition correlated with MCG7 function or with an aberration in mcg7 sequence.

The specification teaches that the coding sequence of mcg7 has been determined from cDNA sequences, and that judging from homology comparisons, the encoded protein has a guanine exchange factor (GEF) activity. No specific activity of the entire protein is described. The prior art teaches that there are different classes of proteins that possess GEF activity. MCG7

is novel in the art and there is no prior art indication of its role in cell function. There is no teaching in the instant application or prior art that an aberration of the mcg7 sequence correlates with a propensity to develop, facilitates or causes any particular condition. Therefore, there is no structural/functional basis for one of skill in the art to envision a particular disease or condition associated with an aberration in the mcg7 sequence, much less which aberration or change would be associated with the condition. Therefore, one of skill in the art would have reasonably concluded applicants weren't in possession of the claimed invention.

Claims 1, 4-5, 8, 11-12, and 15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Each of the claims is drawn towards an isolated nucleic acid encoding a regulator of gene expression (e.g. claims 1 and 8). Some of the claims are more broadly drawn to a gene regulator possessing a guanine nucleotide exchange activity (e.g. claims 4 and 11). This guanine nucleotide exchange factor that is also a gene expression regulator can also be: (i) a nucleotide sequence as set for in SEQ ID NO: 4, (ii) a nucleotide sequence encoding an amino acid sequence of SEQ ID NO: 5, (iii) a nucleotide sequence having at least 40% similarity to the nucleotide sequence set forth in (i) or (ii), and (iv) a nucleotide sequence capable of hybridizing under low stringency to the nucleotide sequence set forth in (i), (ii) or (iii) (e.g. claims 5 and 12).

In many of the claims, the nucleotide sequence can be a "derivative" of the recited sequence. The term "derivative"

Given the extreme breadth of the claims, and the ambiguity of the word "derivative", the rejected claims encompass almost any number of proteins that can function in some fashion as a regulator of gene expression (e.g. signal transduction receptors, chromatin proteins, transcriptional activators, transcriptional repressors, etc.) obtained from literally any source (animal, prokaryotic, plants, protozoan, etc.). The instant specification merely provides a comparison of the nucleotide sequence and deduced amino acid sequence for human mcg7 to a couple of different sequence known in the art (e.g. C. elegans, murine, etc. in Figures 14-15). It does not provide a basis for one of skill in the art to envision a sufficient number of different guanine nucleotide exchange factors that are found in nature to describe the broadly claimed genus. Even for those embodiments limited to 40% similarity, or capable of hybridizing at low stringency, to SEQ ID NO: 4, there is no basis provided by the specification to enable the skilled artisan to envision what other proteins that satisfy the similarity requirement will look like, and still retain mcg7 activity.

The prior art does not offset the deficiencies of the instant specification, as mcg7 appears to be novel in the art. Moreover, the prior art makes clear that it is unpredictable to attempt to determine the structural/functional characteristics of a protein from its primary sequence alone. The relationship between the sequence of a protein and its tertiary structure (in essence the structure which defines its activity), is not well understood and is not predictable as evidenced by Berendsen (Science. 1998, Vol. 282, pages 642-643; see the entire document). This reference teaches that "Thus, one of the "grand challenges" of high-performance computer-predicting the

structure of proteins-acquires much of the flavor of the Holy Grail quest of the legendary knights of King Arthur: It is extremely desirable to possess but extremely elusive to obtain." (Page 643, columns 1-2). Thus, as taught by Berendsen, it is unlikely that one would be able to reliably envision those embodiments that fulfill the similarity or hybridizing limitations and which also retain mcg7 activity.

Given the broad genus of gene regulators encompassed by the claims, and the lack of a means in the instant specification or prior art for envisioning specific embodiments that meet all of the claim limitations, one of skill in the art would not be able to envision a sufficient number of specific embodiments of the claims nucleotide sequences in order to describe the broadly claimed genus of nucleotides encoding gene expression regulators. Therefore, one of skill in the art would reasonably have concluded applicants were not in possession of the claimed invention at the time of filing.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-5, 8, 11-12, 15 and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 8, 11 are vague and indefinite in that the metes and bounds of the term "a derivative" of a gene regulator (e.g. a GEF protein) are unclear. It is unclear the nature and number of steps necessary in order to obtain a "derivative" of a gene regulatory protein. It would be remedial to delete this term from the claim language.

Claim 8 is further indefinite in that the metes and bounds of the phrases "a vector portion" and "a gene portion" are unclear. What is the lower limit for what would satisfy the term " a portion" of a gene or vector? Would a single nucleotide from a vector or gene be able to satisfy this limitation? It would be remedial to amend the claim language to clearly indicate what are the minimum amounts of nucleic acids that can qualify as a "portion" of a gene or vector in context of the claim.

Claim 8 is also indefinite in that it recites "a gene portion comprising a regulator of gene expression". In the context of the invention, the regulator of gene expression is a protein. Yet, the claim appears to specify that a gene or portion thereof comprises a protein. It would be remedial to amend the claim language to clearly indicate that the gene *encodes* the protein.

Claim 11 is likewise indefinite in that it specifies that "said gene portion is a nucleotide exchange factor (GEF)". It would be remedial to amend the claim to indicate the gene sequence *encodes* the GEF protein.

Claim 15 is vague and indefinite in that the metes and bounds of the phrase "a gene regulator having the identifying characteristics of.....MCG7...having...an amino acid sequence of SEQ ID NO: 5" are unclear. It's unclear what exactly are the "identifying characteristics" of MCG7. For example, would molecular weight satisfy the limitation? Would the color of a crystal of the protein satisfy the limitation. It would be remedial to amend the claim language to clearly indicate what is meant by the term "identifying characteristics.

Claim 19 is vague and indefinite in that the use of the phrases "the presence of a single or multiple nucleotide substitution, deletion and/or addition or other aberration to one or both alleles of mcg7" and "such a nucleotide substitution, deletion and/or addition or other aberration"

makes unclear the nature and number of combinations of different alterations of the mcg7 sequence that are permissible. It is further indefinite what other kind of aberration of mcg7 would not fit into the combination of substitutions, deletions and/or additions recited in the claim.

Claim 19 is further indefinite in that the stipulation that the presence of such an alteration in the mcg7 sequence "may" be indicative of a condition or propensity to develop the condition makes it unclear whether the end result of the claim recapitulates the end result stated in the preamble (i.e. detection of a condition caused or facilitated by an aberration in mcg7). Moreover, the limitation of a "propensity to develop" a condition does not have a clear antecedent basis in the steps of the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the

reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1, 4, 8, 11 and 15 rejected under 35 U.S.C. 102(e) as being anticipated by Bowtell (U.S. Patent No. 5,843,646; see the entire document).

The rejected claims are so broadly drawn as to read on any nucleic acid encoding a guanine nucleotide exchange factor, or any vector comprising the nucleic acid encoding the protein. For example, claim specifies a nucleic acid encoding a gene regulator "having the identifying characteristics of....MCG7...and having respective amino acid sequences of...SEQ ID NO: 5..." Read in a reasonably broad fashion, this claim reads on any nucleic acid encoding any protein.

Bowtell teaches nucleic acids and vectors comprising such nucleic acids that encode the murine Son of Sevenless protein, which is a guanine nucleotide exchange factor involved in signal transduction pathways that activate several different genes (e.g. Abstract).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gerald G Leffers Jr. whose telephone number is (703) 308-6232. The examiner can normally be reached on 9:30am-6:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 305-7939 for regular communications and (703) 305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gerald G Leffers Jr.
Examiner
Art Unit 1636

Ggl
May 22, 2003